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Multicenter performance evaluation of the new Elecsys Vitamin D total III assay

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Background

- Vitamin D is an essential nutrient that plays a role in numerous physiological functions; it is estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency.[1–6]
- Vitamin D exists in two bioequivalent forms, vitamin D2 and D3, which are converted to 25-hydroxyvitamin D (25[OH]D) in the liver; the serum concentration of total 25(OH)D (the sum of 25[OH]D2 and 25[OH]D3) is the most reliable indicator of vitamin D status.[4–6]
- Isotope dilution liquid chromatography tandem mass spectrometry (ID-LC-MS/MS) is the gold standard for measuring total 25(OH)D; however, most routine analyses are performed using automated assays.[6–8]
- The new Elecsys® Vitamin D total III assay (Roche Diagnostics International Ltd, Rotkreuz, Switzerland) is intended for the quantitative determination of total 25(OH)D in serum and plasma; it has been standardized using internal calibrators that are traceable to the ID-LC-MS/MS 25(OH)D Reference Measurement Procedure.[7–10]

Objectives

- **To evaluate the analytical performance of the new Elecsys Vitamin D total III assay (cobas e 601 analyzer), conduct method comparisons versus other commercially available assays and between serum and plasma matrices, and calculate diagnostic accuracy versus reference ID-LC-MS/MS values.**

Methods

- The Elecsys Vitamin D total III assay was evaluated under routine conditions at three laboratories (Heidelberg, Germany; Habach, Germany; Baltimore, MD, USA) from February–March 2020.
- Repeatability and intermediate precision testing was conducted at all sites using five anonymized human serum pools (HSPs) and two PreciControl (PC) materials over five days and one reagent lot (per CLSI-EP05-A3 guidelines); standard deviation (SD) and coefficient of variation (CV) values were calculated and compared with predefined acceptance criteria.
- Method comparisons versus other commercially available assays and concordance analyses were performed at two sites (Heidelberg and Baltimore) using a Centers for Disease Control and Prevention (CDC) serum sample verification panel with reference ID-LC-MS/MS values; between-method differences were assessed using unweighted Deming regression analysis.
- A separate serum versus plasma comparison analysis with the Elecsys Vitamin D total III assay was conducted at a single site (St Louis, MO, USA) using samples from 462 apparently healthy adults; between-matrix differences were assessed using Passing-Bablok regression analysis.

Results

Analytical performance

- SD and CV values for repeatability and intermediate precision met the predefined acceptance criteria across all three sites (**Table 1**).

Table 1. Repeatability and intermediate precision of the Elecsys Vitamin D total III assay*

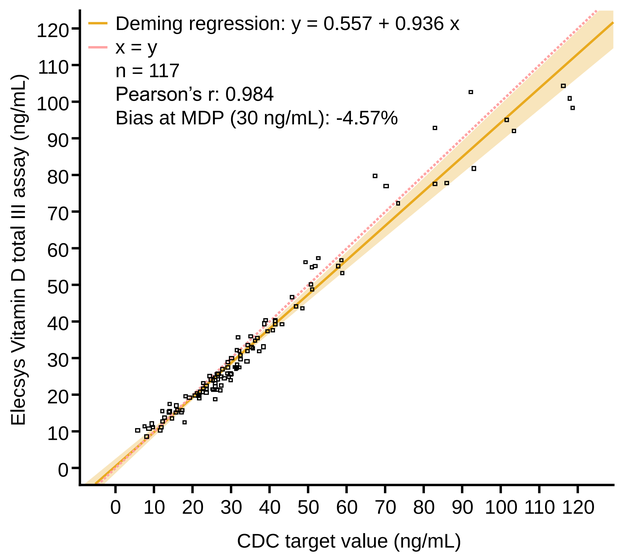
Sample‡	n	Mean vitamin D concentration, ng/mL	Repeatability§	Intermediate precision¶
HSP1	75	16.8–18.4	SD, 0.870–1.07	SD, 1.14–1.77
HSP2	74**	32.1–34.6	CV%, 2.33–5.19	CV%, 3.22–7.83
HSP3	74**	61.7–64.3	CV%, 2.76–5.97	CV%, 3.16–8.37
HSP4	74**	80.2–82.8	CV%, 2.51–6.43	CV%, 3.10–7.66
HSP5	75	94.5–98.0	CV%, 1.58–2.76	CV%, 2.00–4.13
PC1	75	19.8–21.1	SD, 0.875; CV%, 3.91–6.13	SD, 1.05; CV%, 5.35–9.71
PC2	75	38.3–40.1	CV%, 2.50–5.61	CV%, 3.18–6.87

*Range of results shown across all three sites; ‡HSPs and PCs were obtained from Roche Diagnostics International Ltd; §Predefined acceptance criteria for repeatability: ≤20.0 ng/mL, SD ≤1.6 ng/mL; >20.0 ng/mL, CV ≤8.0%; ¶Predefined acceptance criteria for intermediate precision: ≤20.0 ng/mL, SD ≤2.2 ng/mL; >20.0 ng/mL, CV ≤11.0%; **One sample was excluded according to predefined study parameters.
CV, coefficient of variation; HSP, human serum pool; PC, PreciControl; SD, standard deviation.

Method comparison

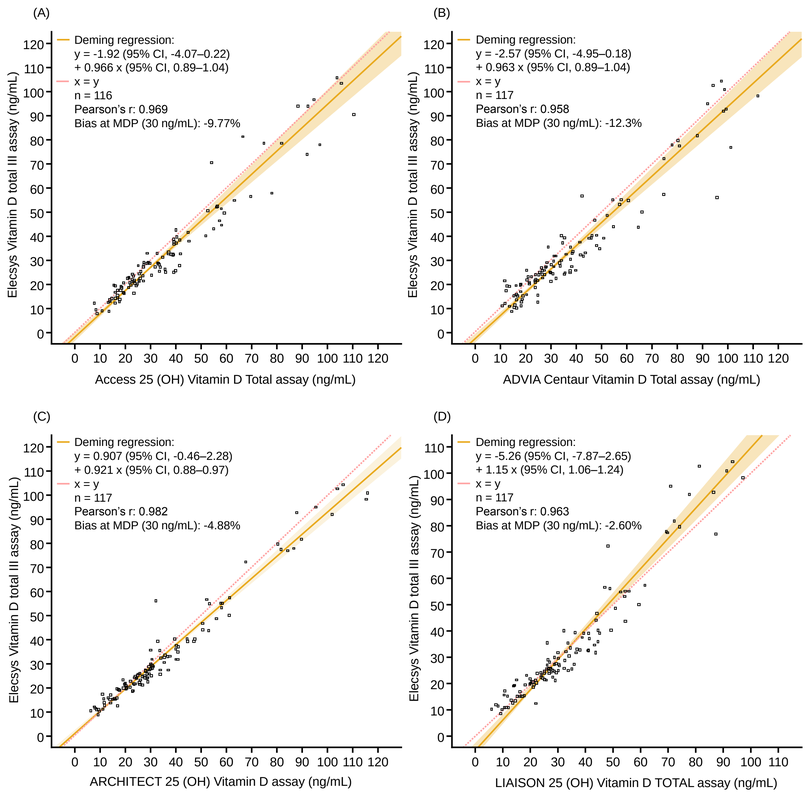
- The Elecsys Vitamin D total III assay showed agreement with the CDC ID-LC-MS/MS verification panel target values (across-site range for Pearson's r: 0.960–0.986; example shown in **Figure 1**).
- Agreement was also observed between the Elecsys Vitamin D total III assay and the comparator assays (Pearson's r: 0.958–0.982; **Figure 2**).

Figure 1. Comparison of the Elecsys Vitamin D total III assay versus CDC ID-LC-MS/MS verification panel target values (Heidelberg site)



CDC, Centers for Disease Control and Prevention; ID-LC-MS/MS, isotope dilution liquid chromatography tandem mass spectrometry; MDP, medical decision point.

Figure 2. Method comparison of the Elecsys Vitamin D total III assay versus other commercially available assays: (A) Access 25 (OH) Vitamin D Total; (B) ADVIA Centaur Vitamin D Total; (C) ARCHITECT 25-OH Vitamin D; and (D) LIAISON 25 OH Vitamin D TOTAL assays



CDC, Centers for Disease Control and Prevention; CI, confidence interval; ID-LC-MS/MS, isotope dilution liquid chromatography tandem mass spectrometry; MDP, medical decision point; OH, hydroxy.

Concordance analysis

- The Elecsys Vitamin D total III assay showed concordance with the CDC ID-LC-MS/MS verification sample set, correctly identifying 100%, 89.5%, and 85.5% of samples deficient, insufficient, and sufficient in vitamin D, respectively (**Table 2**).

Table 2. Concordance of the Elecsys Vitamin D total III assay versus other commercially available assays in the CDC ID-LC-MS/MS verification panel

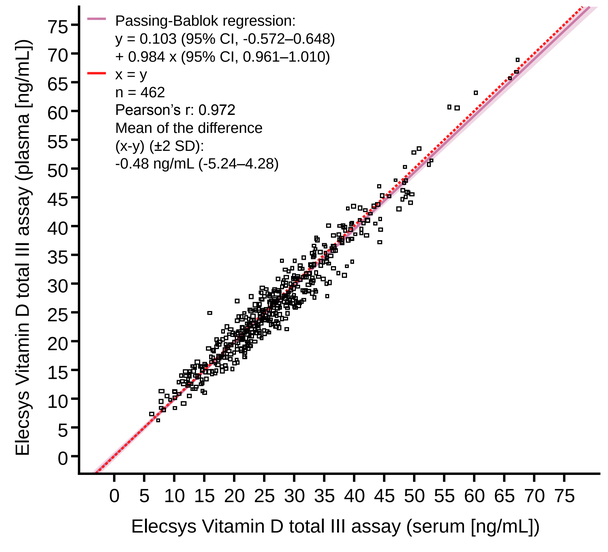
		Concordant samples, n (%)				
CDC vitamin D group	**n**	**Elecsys Vitamin D total III**	**Access 25 (OH) Vitamin D Total**	**ADVIA Centaur Vitamin D Total**	**ARCHITECT 25-OH Vitamin D**	**LIAISON 25 OH Vitamin D TOTAL**
Deficient (<20 ng/mL)	24	24 (100.0)	23 (95.8)	21 (87.5)	24 (100.0)	23 (95.8)
Insufficient (20–30 ng/mL)	38	34 (89.5)	23 (60.5)	24 (63.2)	33 (86.8)	29 (76.3)
Sufficient (>30 ng/mL)	55	47 (85.5)	45 (83.3)*	51 (92.7)	52 (94.5)	50 (90.9)
Total	117	105 (89.7)	91 (78.4)*	96 (82.1)	109 (93.2)	102 (87.2)

*One sample was outside the measuring range of the Access 25 (OH) Vitamin D Total assay, thus there were 54 samples in the sufficient group and 116 total samples included in the analysis for this assay.
CDC, Centers for Disease Control and Prevention; ID-LC-MS/MS, isotope dilution liquid chromatography tandem mass spectrometry; OH, hydroxy.

Serum versus plasma comparison

- The Elecsys Vitamin D total III assay demonstrated comparable analytical performance in serum versus plasma samples from apparently healthy individuals (Pearson's r: 0.972; **Figure 3**).

Figure 3. Comparison of Elecsys Vitamin D total III assay results in serum and plasma samples



CI, confidence interval; SD, standard deviation.

Conclusion

- **The Elecsys Vitamin D total III assay demonstrated good analytical performance and compared favorably with other commercially available assays, supporting its use as a clinical aid in the determination of vitamin D sufficiency.**

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